

Remarks

Claims 1-66, 94, 97-103, 110-112 and 115 have been cancelled previously. Claims 81-85 and 87-93 have been withdrawn. Claims 67-80, 86, 95, 96, 104-108, 113 and 114 have been amended previously. Claims 67-80, 86, 95, 96, 104-109, 113 and 114 are being examined in the instant application. No amendments to the claims are made presently.

The Applicants are pleased that the Patent Office considers the previous amendments to the specification and claims to have obviated the specification and claim objections of record. Likewise, the Applicants are pleased that the Patent Office found the Applicant's assurances that the Deposit was made under the terms of the Budapest Treaty sufficient to obviate the 35 USC 112 first paragraph rejection of record. Additionally, the Applicants are pleased that the Patent Office found that the cancellation of relevant claims in copending application USSN 09/898,195 to obviate the provisional double patenting rejection of record.

35 USC 102(b) Rejection

Claims 67-80, 86, 95, 96, 104-109, 113 and 114 are rejected under 35 USC 102(b) as being anticipated by Peach et al. (WO 98/33513) as evidenced by Cohen et al. (US 2003/0083246).

The Patent Office acknowledges, on page 4 of the above referenced Office Action, "that WO98/33513 teaches that the sequence of LEA29Y is set forth in SEQ ID NO:1 (where Xaa is "Y" and Yaa is "E"), and that the amino acid sequence of SEQ ID NO:1 is not the same as instant SEQ ID NO:4 or the amino acid sequence set forth in instant Figure 7." The Applicants agree with the Patent Office and assert that Peach et al. (WO 98/33513), alone or as evidenced by Cohen et al., does not expressly or inherently anticipate the instantly claimed CTLA4 mutant molecules.

The Patent Office expresses concerns about the identity of the instantly claimed invention, relating to how the instantly claimed invention and a molecule in Peach et al. (WO 98/33513) have been named. Before directly addressing these concerns, the Applicants wish to direct the Patent Office to the claims being examined in the instant application. These claims, along with the disclosure in WO 98/33513, must drive the novelty analysis.

Each claim being examined in the instant application refers to a disclosed amino acid sequence and defines the CTLA4 mutant molecule being claimed by that amino acid sequence. In each claim, the claimed CTLA4 mutant molecule has two mutations in the CTLA4 extracellular domain relative to the wild type CTLA4 extracellular domain: a mutation of leucine at position 104 to glutamic acid; and a mutation of alanine at position 29 to tyrosine (using the numbering system of Figure 7 of the instant application). No claim claims a CTLA4 mutant molecule defined by a name.

The term "LEA29Y" is not used in any claim. The claims clearly define the invention being claimed, and that definition is by sequence.

The Patent Office states, on page 3 of the above referenced Office Action, that "[n]o objective evidence that the LEA29Y molecule taught by Peach et al. is different [from] the instantly claimed LEA29Y molecule has been presented by the Applicant," and that "[a]bsent any factual evidence to clarify the identity of the claimed molecule, the [102(b)] rejection is maintained essentially for the reasons of record." The Applicants submit that the sequence in the instant application *is the evidence* defining an instantly claimed CTLA4 mutant molecule, and that the sequence *is the identity* of a claimed CTLA4 mutant molecule. There is no clarification needed. The Applicants submit that, equally importantly, the sequence in the prior art reference WO98/33513 is the evidence defining a molecule in that prior art reference. To anticipate an instantly claimed molecule which is defined by sequence, a prior art molecule must have the same sequence as the instantly claimed molecule. As noted by the Patent Office, the sequences of the instantly claimed CTLA4 mutant molecules are not in the prior art of record.

The Applicants direct the Patent Office to SEQ ID NO:4 and Figure 7 of the instant application for clear factual evidence of the identity of a claimed CTLA4 mutant molecule comprising an amino acid sequence beginning with methionine at position 27 and ending with lysine at position 383 of SEQ ID NO:4 or an amino acid sequence beginning with alanine at position 26 and ending with lysine at position 383 of SEQ ID NO:4 (claim 76). Using the numbering system of Figure 7 of the instant application, this instantly claimed CTLA4 mutant molecule has a mutation of leucine at position 104 to glutamic acid, and a mutation of alanine at position 29 to tyrosine. To the contrary, using the same numbering system of Figure 7 of the instant application, the prior art Peach et al. (WO98/33513) discloses a CTLA4 mutant molecule which has a mutation at position 105 to glutamic acid, and a mutation at position 28 to tyrosine. The disclosure of the prior art reference does not contain each element of the sequence of the instantly claimed molecule and, therefore, cannot be anticipatory. ("Anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim." *Lindermann Maschinenfabrik GMBH v. American Hoist & Derrick*, 221 USPQ 481, 485 (Fed. Cir. 1984)). Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office, on page 3 of the above-referenced Office Action, expresses confusion with the concept that a molecule can be referred to by the same name as another molecule with a different amino acid sequence. The Patent Office is unclear about how two different disclosed sequences in two different documents ended up with the same name and wishes to determine "which of the two definitions of molecular identity is correct: either (a) the same molecule is disclosed as having two different amino acid sequences in Peach et al. (WO 98/33513) and the

instant application, e.g. due to a sequencing error, or (b) two different molecules have been given the same name by the same group of Inventors.”

The Applicants respectfully submit that determining which of the two sequences “correctly” defines “LEA29Y” is irrelevant in determining the novelty of the instantly claimed invention. What is relevant in determining the novelty of the instantly claimed invention is what sequence was disclosed in the prior art reference and what sequence is now being claimed. A name used to refer to an invention is not important; it is the elements of the claimed invention and not the given name that defines the claimed invention. (See, eg., *Ethyl Molded Products Company v. Betts Packaging, Inc.*, 9 U.S.P.Q.2D 1001, 1011 (1988) “In viewing the prior art, as well as determining infringement, the names given to parts of a closure are not important.... Thus, it is the actual structure and function of a closure part that is important, and not the name given to it by the defendant.”) Sequence defines a claimed CTLA4 mutant molecule, and, as acknowledged by the Patent Office, the prior art sequence set forth in SEQ ID NO:1 of WO98/33513 is not the same as the claimed molecule defined by instant SEQ ID NO:4 or Figure 7. Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Patent Office states, on page 4 of the above referenced Office Action that an ordinary artisan at the time of the invention would have recognized that there was a discrepancy between the sequences set forth in SEQ ID NO:1 and Figure 7 of WO98/33513 and the description of the positions mutated in the CTLA4 sequence provided on page 19 of WO98/33513. To support this assertion, the Patent Office states that “[f]or example, page 19 identifies the CDR1 loop of CTLA4 as S25 to R33, whereas Figure 7 has S26 and R34.” The Patent Office seems to be asserting that because of this alleged discrepancy the instantly claimed invention was disclosed in WO98/33513 to the ordinary artisan. Without commenting on whether the ordinary artisan would indeed have recognized the alleged discrepancy, the Applicants respectfully disagree with the Patent Office’s basis for the rejection.

The Patent Office refers to an alleged discrepancy in WO98/33513 in the identification of the CDR1 loop, presumably relating to the mutation at position 29 from alanine to tyrosine in the instantly claimed invention. The instantly claimed invention has two mutations: one at position 29, which is in the CDR1 loop; and one at position 104, which is not in the CDR1 loop. The rejection does not address the mutation at position 104. A proper rejection addresses all elements of the claimed invention. The Applicants submit that this rejection is inadequate because all elements of the claimed invention are not addressed. The Applicants assert that the instantly claimed molecules meet the legal standard for novelty.

The Applicants direct the Patent Office to the Applicants' June 1, 2004 response for further discussion regarding the rejection under 35 USC 102(b), which will not be reiterated here.

Conclusion

For all of the above-stated reasons, the Applicants respectfully request that the Patent Office withdraw the art rejections under 35 U.S.C. 102(b).

The Examiner is invited to contact the undersigned if there are any questions relating to the prosecution of this application.

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,

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A handwritten signature in cursive script, reading "Audrey F. Sher", written over a horizontal line.

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